IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IMMUNEX CORPORATION; AMGEN MANUFACTURING, LIMITED; and HOFFMANN-LA ROCHE INC.; Plaintiffs, v. SANDOZ INC.; SANDOZ INTERNATIONAL GMBH; and SANDOZ GMBH Defendants.	Honorable Claire C. Cecchi, U.S.D.J. Civil Action No. 16 CV 1118 (CCC)(MF)

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

OF COUNSEL:
George C. Lombardi
Maureen L. Rurka
Julia Mano Johnson
WINSTON & STRAWN LLP
35 West Wacker Drive
Chicago, Illinois 60601-9703
(312) 558-5600

WINSTON & STRAWN LLP
The Legal Center
One Riverfront Plaza, Suite 730
Newark, NJ 07102
(973) 848-7676
James S. Richter
Melissa Steedle Bogad

Attorneys for Defendants Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH

Merritt D. Westcott
Melinda K. Lackey
WINSTON & STRAWN LLP
1111 Louisiana Street, 25th Floor
Houston, Texas 77002-5242
(713) 651-2600

TABLE OF CONTENTS

Page

I. INTRODUCTION 1

II. TECHNICAL BACKGROUND 3

A. Immunoglobulins 3

B. TNF and TNF Receptors 5

C. Fusion Proteins and Etanercept 7

III. LEGAL STANDARDS 8

IV. ARGUMENT 11

A. Submarine Patents: The "Domains" Claim Terms Exclude The Hinge. 11

1. The Ordinary Meaning Of The Term "Domain" Excludes The Hinge. 12

2. Plaintiffs' Construction Contradicts The Plain And Ordinary Meaning 19

B. '182 Patent: The Term "Specifically Binds TNF" Should Be Construed To Require Only In Vitro TNF Binding, Consistent With The Intrinsic Record. 21

C. '522 Patent: The Polynucleotide Term Requires That The Polynucleotide Encode Only The Claimed Protein 25

D. Psoriasis Patents: "Patient" 26

E. Psoriasis Patents: "Psoriasis" & "Ordinary Psoriasis" 29

1. Sandoz's Construction Recognizes that Psoriasis and Psoriatic Arthritis Are Separate Diseases 30

2. Sandoz's Constructions Avoid Confusion and Overlap Between Terms, Which Would Render These Terms Indefinite 33

F. Psoriasis Patents: "Psoriatic Arthritis" 34

G. Psoriasis Patents: "Plaque Psoriasis" 35

V. CONCLUSION 36

TABLE OF AUTHORITIES

CASES

Bayer Pharma AG v. Watson Labs., Inc.,
No. 12-1726-LPS-CJB, 2014 WL 4954617 (D. Del. Sept. 30, 2014) 10

Bristol-Myers Squibb Co. v. Mylan Pharms. Inc.,
No. 09-651-LPS, 2012 WL 1753670 (D. Del. May 16, 2012) 9

Dayco Prods., Inc. v. Total Containment, Inc.,
258 F.3d 1317 (Fed Cir. 2001) 23

Graphics Properties Holdings, Inc. v. Asus Computer Int'l, Inc.,
No. 12-210-LPS, 2014 WL 4929340 (D. Del. Sept. 29, 2014) 10

Helmsderfer v. Bobrick Washroom Equipment, Inc.,
527 F.3d 1379 (Fed. Cir. 2008) 17

Hill-Rom Servs., Inc. v. Stryker Corp.,
755 F.3d 1367 (Fed. Cir. 2014) 20

Interval Licensing LLC v. AOL, Inc.,
766 F.3d 1364 (Fed. Cir. 2014) 10

Johnson Worldwide Assocs., Inc. v. Zebco Corp.,
175 F.3d 985 (Fed. Cir. 1999) 28-29

Libel-Flarsheim Co. v. Medrad, Inc.,
358 F.3d 898 (Fed. Cir. 2004) 21

Liberty Ammunition, Inc. v. United States,
835 F.3d 1388 (Fed. Cir. 2016) 29-30, 34

Markman v. Westview Instruments, Inc.,
52 F.3d 967 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996) 8

Multiform Desiccants, Inc. v. Medzam, Ltd.,
133 F.3d 1473 (Fed. Cir. 1998) 27

Paragon Solns., LLC v. Timex Corp.,
566 F.3d 1075 (Fed. Cir. 2009) 25

Phillips v. AWH Corp.,
415 F.3d 1303 (Fed. Cir. 2005) 9

Quaker City Gear Works, Inc. v Skil Corp.,
747 F.2d 1446 (Fed. Cir. 1984) 17

Roy-G-Giv Corp. v. ABB, Ltd.,
63 F. Supp. 3d 690 (E.D. Tex. 2014) 21

Sinorgchem Co., Shandong v. Int'l Trade Comm'n,
511 F.3d 1132 (Fed. Cir. 2007) 26-27, 35

SmithKline Beecham Corp. v. Apotex Corp.,
403 F.3d 1331 (Fed. Cir. 2005) 9

Thorner v. Sony Computer Entm't Am. LLC,
669 F.3d 1362 (Fed. Cir. 2012) 12, 20

Vehicular Techs. Corp. v. Titan Wheel Intern., Inc.,
212 F.3d 1377 (Fed. Cir. 2000) 26

Vitronics Corp. v. Conceptronic, Inc.,
90 F.3d 1576 (Fed. Cir. 1996) 23

STATUTES

35 U.S.C. § 112 .....10, 18, 29, 34

America Invents Act § 4(c), Pub. L. No. 112-29 10

RULES

37 C.F.R. 3.37(b) 2

MISCELLANEOUS

https://www.researchgate.net/figure/10840382_fig5_Figure-1-Membrane-bound-TNF-memTNF-and-soluble-TNF-sTNF-derived-thereof-both-bind.....6

TABLE OF ABBREVIATIONS

Abbreviation	Term
BPCIA	The Biologics Price Competition and Innovation Act
’182 patent	U.S. Patent No. 8,063,182
’522 patent	U.S. Patent No. 8,163,522
’225 patent	U.S. Patent No. 7,915,225
’605 patent	U.S. Patent No. 8,119,605
’631 patent	U.S. Patent No. 8,722,631
Submarine patents	The ’182 and ’522 patents
Psoriasis patents	The ’225, ’605, and ’631 patents
IgG	Immunoglobulin of class G
C	Constant region of an immunoglobulin
V	Variable region of an immunoglobulin
TNF	Tumor necrosis factor
TNFR	Tumor necrosis factor receptor
PsO	Psoriasis
PsA	Psoriatic arthritis

I. INTRODUCTION

This case arises under the BPCIA and relates to a drug called "etanercept." Immunex markets etanercept under the brand name "Enbrel." Sandoz has received FDA approval to market a biosimilar version of Enbrel under an abbreviated biologics license application or "ABLA." Sandoz will market its etanercept product under the brand name "Erelzi."

There are two sets of patents at issue here: the '182 and '522 patents, or "submarine patents" (Bogad Exs. 1-2), which expire on November 22, 2028 and April 24, 2029, respectively, and the '225, '605, and '631 patents, or "psoriasis patents" (Bogad Exs. 3-5), which expire on November 24, 2019.[1] The submarine patents claim a protein and a method of making a protein that is made up of part of an immunoglobulin and part of a tumor necrosis factor receptor, or "TNFR." The psoriasis patents relate to methods of treating three types of psoriasis with etanercept: psoriasis/ordinary psoriasis, plaque psoriasis, and psoriatic arthritis.

Immunex developed Enbrel in the mid-1990s and obtained several other patents covering the compound. *See, e.g.*, U.S. Patent Nos. 5,395,760 (Bogad Ex. 6, "Smith '760"); 5,605,690 (Bogad Ex. 7). The last of those patents expired in

[1] Citations to "Bogad Ex." refer to the exhibits referenced in the Declaration of Melissa Steedle Bogad in support of Defendants' Opening Claim Construction Brief, filed contemporaneously.

2014. At the same time Immunex was developing etanercept, Plaintiff Roche was also working on the same type of fusion proteins and filed patent applications, two of which ultimately issued as the submarine patents. Because Roche's applications were filed before 1995, their existence was never made public until 2011 and 2012, when the submarine patents issued, and after Sandoz had invested significant time and expense in developing Erelzi.

Although Roche filed the applications, Immunex ended up owning them pursuant to an agreement between Roche and Immunex executed in 2004. In that agreement, all substantial rights to the patent applications, including the right to prosecute those applications and to control this litigation, were transferred to Immunex. *See* Bogad Ex. 8, '182 File History at Oct. 6, 2004 Statement under 37 C.F.R. 3.37(b), Revocation of Power of Attorney and Power of Attorney by Assignee; Dkt. 7, Complaint, at ¶¶ 1, 11, 12, 13. Thus, after enjoying a full period of patent protection for Enbrel with its own patents, Immunex obtained another 17 years of patent coverage by obtaining Roche's patents.

The parties dispute the meaning of three claim terms in the submarine patents and five claim terms in the psoriasis patents. In all cases, Sandoz's constructions follow the well-established principles of claim construction, applying the plain and ordinary meaning of the terms as understood by a person of ordinary skill in the art

("POSA"), consistent with the intrinsic record. Plaintiffs, on the other hand, ignore the plain meaning of terms and disregard express definitions in the specification. In addition, several of Plaintiffs' constructions are vague and provide insufficient guidance as to the meaning of the terms. Sandoz's constructions, which follow the Federal Circuit's rules for claim construction, should be adopted.

II. TECHNICAL BACKGROUND

Below is a brief explanation of the relevant technical background.

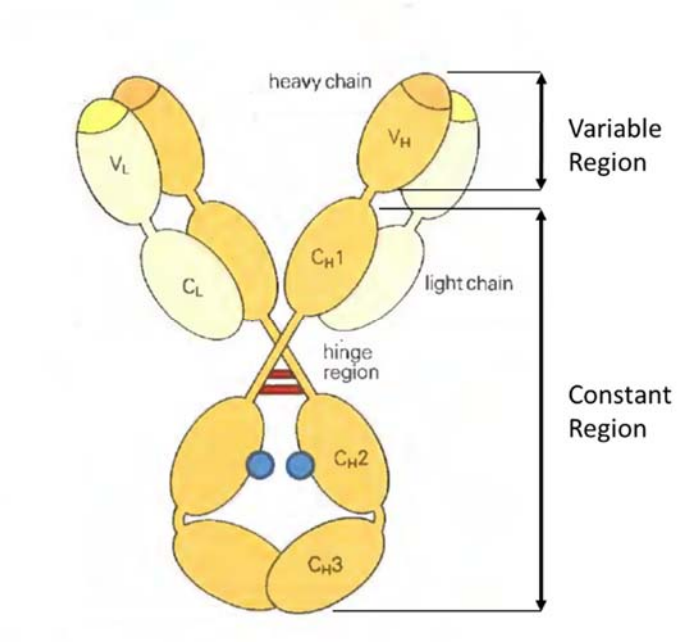
A. Immunoglobulins

The submarine patents cover a fusion protein and a process for making it. Fusion proteins are common and basic proteins that are made up of parts of two or more distinct proteins that are fused or pieced together, akin to fitting together two or more pieces of Legos. Fusion proteins can be pieced together in order to get the useful properties from each of the separate proteins. The claimed fusion protein here is made up of part of an immunoglobulin and part of a Tumor Necrosis Factor Receptor or "TNFR."

Immunoglobulins, commonly referred to as antibodies, are proteins that are produced by the immune system typically to bind to and neutralize foreign organisms or "pathogens" introduced into the body. Such pathogens include bacteria

and viruses. Stein Decl. at ¶ 18.[2] In humans, the most common class of immunoglobulin is called "IgG." *Id.* at ¶ 19. IgGs come in various types. Specifically, IgG may be further classified into four subclasses of distinct immunoglobulins, which are called IgG1, IgG2, IgG3, and IgG4. *Id.* Here, the submarine patent claims are directed generally to IgG or in some cases, specifically IgG1.

All IgG immunoglobulins, including IgG1, are made up of long chains of chemicals called amino acids. IgGs share a characteristic structure, as illustrated below, that forms a distinctive Y-shape. *Id.* at ¶ 20



Stein Ex. 5 at Fig. 5.8 (annotations added).

[2] Citations to the "Stein Decl." and "Stein Ex." refer to the Declaration of Kathryn E. Stein, Ph.D. on Claim Construction and its exhibits, filed contemporaneously.

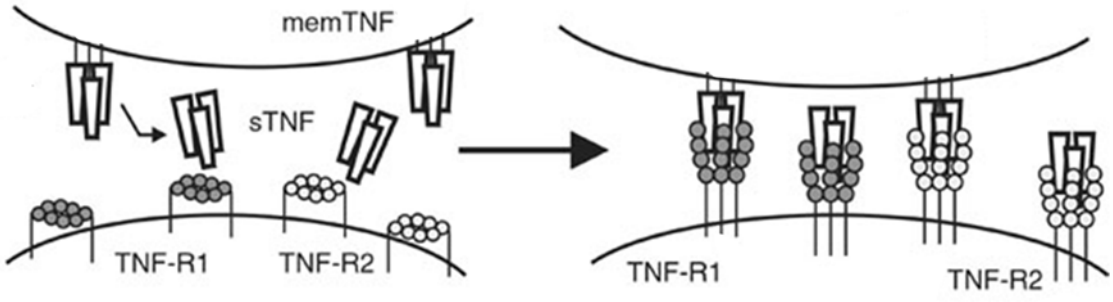
Each of the heavy chains and light chains of the IgG immunoglobulin has a variable region and a constant region. Stein Decl. at ¶ 21. The variable regions of the heavy and light chains are the tips of the Y-shaped protein, denoted as V_L and V_H. These combine to form the two sites on an IgG molecule that bind to proteins called "antigens" in the body. *Id.* V_L and V_H are called "variable" because their amino acid sequences vary among immunoglobulins.

The constant regions of the heavy chains is made up of C_H1, C_H2, and C_H3, and comprises the rest of the Y-shaped protein. The constant region activates the other parts of the immune system to neutralize the pathogen. *Id.* at ¶ 22. It is called "constant" because the amino acid sequence is highly similar in immunoglobulin molecules of its class. In other words, all IgG proteins have highly similar constant region amino acid sequences. The hinge is an area within the constant region of the IgG immunoglobulin that is between C_H1 and C_H2 to form the Y-shaped protein. *Id.*

B. TNF and TNF Receptors

Tumor Necrosis Factor-α and –β, or "TNF", are proteins that act on cells by binding to certain receptors that appear on the surface of cells. TNF can appear on the surface of other cells or can be floating free in the body. TNF is involved in various conditions, including immune responses and inflammation. TNF is known to have beneficial effects, but excessive TNF in the body is also known to have significant negative effects.

TNF can bind to different things, including certain antibodies that contain antigen binding sites specific to TNF, as well as to specific TNF receptor proteins, or "TNFRs," that are on the surface of a cell. Below is a diagram of how free TNF, or "sTNF," and cell-bound TNF, or "memTNF," bind to TNFRs on the surface of other cells:



Adapted from https://www.researchgate.net/figure/10840382_fig5_Figure-1-Membrane-bound-TNF-memTNF-and-soluble-TNF-sTNF-derived-thereof-both-bind, last accessed 12/1/16.

There are two TNFRs—the p55 and the p75 TNFR, indicated as "TNF-R1" and "TNF-R2," respectively in the above diagram. Bogad Ex. 9, '182 file history, at May 19, 1995 Original Abstract. The "extracellular region" of a TNFR consists of the portion of the TNFR that protrudes outside of the cell. The p55 and p75 TNFRs are referred to as such based on their weight: 55 kilodaltons and 75 kilodaltons, respectively. The submarine patents are directed to the p75 TNFR.

TNFRs can be used, either in the lab or in the body, to bind TNF, and this was recognized in the art before the applications from which the submarine patents were filed. The TNFR can be used to bind TNF in order to avoid the negative effects of

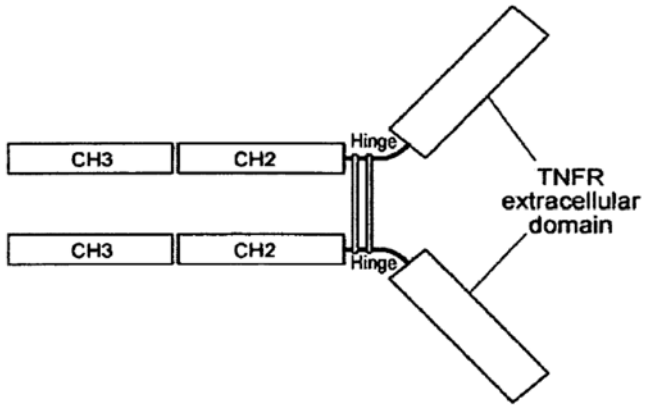
TNF in the body, as well as to perform diagnostic tests on, *e.g.*, blood samples. As stated in Smith '760:

> Because of the ability of TNF to specifically bind TNF receptors (TNF-Rs), purified TNF-R compositions will be useful in diagnostic assays for TNF, as well as in raising antibodies to TNF receptor for use in diagnosis and therapy. In addition, purified TNF receptor compositions may be used directly in therapy to bind or scavenge TNF, thereby providing a means for regulating the immune activities of this cytokine.

Bogad Ex. 6, Smith '760, 2:67-3:6.

C. Fusion Proteins and Etanercept

Etanercept is a fusion protein that consists of (1) the CH2 and CH3 domains of an IgG1 immunoglobulin, (2) the hinge region of IgG1, and (3) the extracellular region of two p75 TNFRs. Its basic structure is depicted below:



Bogad Ex. 10, '182 file history, Feb. 28, 2008 Appeal Brief at 13.

The creation of fusion proteins that combine proteins such as a TNFR with fragments of human immunoglobulins, particularly IgGs, was well known in the art by 1990. Indeed, multiple groups were investigating the fusion of human IgGs to

different types of proteins, including TNFRs. *See, e.g.*, Bogad Ex. 6, Smith '760 at 10:53-61. Multiple configurations are possible, including structures that include or exclude domains or all or part of the hinge region. *See, e.g.*, Bogad Ex. 12, '182 file history, Oct. 3, 2006 Amend. & Req. Reconsid., at 13-14; *see also id.* at 16-17 (arguing that a person of skill in the art would not have expected a dimeric protein to retain TNF-binding activity); Bogad Ex. 10, '182 file history, Feb. 28, 2008 Appeal Brief at 43-44 (arguing same); Bogad Ex. 13, '522 file history, Sept. 8, 2010 Amend & Req. Reconsid. at 26-27 (arguing same); *id.* at 24-25 (discussing various reasons why the person of ordinary skill in the art would prefer constructs without the hinge).

The TNFR portion of etanercept binds to excess TNF in the body, which makes etanercept useful for treating a variety of diseases that occur due to excess TNF in the body. Among these are rheumatoid arthritis and various types of psoriasis. *See* Bogad Ex. 11, Enbrel® Label (2009) at 2.

III. LEGAL STANDARDS

The construction of patent claim terms is a question of law to be determined by the Court. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). Claim terms "are generally given their ordinary and customary meaning . . . [which is] the meaning that the term would have to a

person of ordinary skill in the art in question at the time of the invention." *Bristol-Myers Squibb Co. v. Mylan Pharms. Inc.*, No. 09-651-LPS, 2012 WL 1753670, at *1 (D. Del. May 16, 2012) (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13) (Fed. Cir. 2005) (internal quotation marks omitted).

The intrinsic evidence—the patent itself, including the claims and the specification, as well as the prosecution history—"'is the most significant source of the legally operative meaning of disputed claim language.'" *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1338 (Fed. Cir. 2005) (citation omitted). "The patent specification 'is always highly relevant to the claim construction analysis.'" *Bristol-Myers Squibb Co.*, 2012 WL 1753670, at *1 (citation omitted). The context of the words surrounding the claim must also be considered. *Id.* at *2 (citing *Phillips*, 415 F.3d at 1314).

Where useful, a court also may "rely on extrinsic evidence, which consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Phillips*, 415 F.3d at 1317 (quotations and citations omitted). The Federal Circuit has stated that "extrinsic evidence in the form of expert testimony can be useful to a court for a variety of purposes, such as to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects

of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* at 1318.

Indefiniteness determinations can be made as part of claim construction. *See, e.g.*, *Graphics Properties Holdings, Inc. v. Asus Computer Int'l, Inc.*, No. 12-210-LPS, 2014 WL 4929340, at * 6 (D. Del. Sept. 29, 2014). Patent applicants must satisfy the Patent Act's definiteness requirement by "particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention." 35 U.S.C. § 112, ¶ 2.[3] "Like claim construction, indefiniteness is a question of law for the court." *Bayer Pharma AG v. Watson Labs., Inc.*, No. 12-1726-LPS-CJB, 2014 WL 4954617, at * 4 (D. Del. Sept. 30, 2014). "Indefiniteness is to be evaluated from the perspective of someone skilled in the relevant art at the time the patent was filed." *Id.* at *3.

[3] Paragraph 2 of 35 U.S.C. § 112 was replaced with newly designated § 112(b) when § 4(c) of the America Invents Act ("AIA"), Pub. L. No. 112-29, took effect on September 16, 2012. However, because the application resulting in the '551 patent was filed before that date, we still refer to the pre-AIA version of § 112. *See Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1369 n.5 (Fed. Cir. 2014).

IV. ARGUMENT

A. Submarine Patents: The "Domains" Claim Terms Exclude The Hinge.

Claim Terms[4]	Immunex's Proposal	Sandoz's Proposal
"all of the **domains** of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region" "all of the **domains** of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region"	"'-hinge-CH2-CH3' region of a human [IgG/IgG1]"	"the CH2 and CH3 domains of human [IgG/IgG1]"

The parties agree that the claim phrase "all of the domains of the constant region of a human immunoglobulin IgG [or IgG1] heavy chain other than the first domain of said constant region" should be construed according to its plain and ordinary meaning to a POSA. As reflected below, the only dispute concerns whether a POSA would consider a "hinge" to be included among the "domains of the constant region of a human immunoglobulin IgG [or IgG1] heavy chain." According to the

[4] Bogad Ex. 1, '182 patent, at claims 1-36; Bogad Ex. 2, '522 patent at claims 1-3, 7-10.

plain and ordinary meaning of the term "domain," the hinge is not a domain. Defendants' proposed construction is therefore correct.

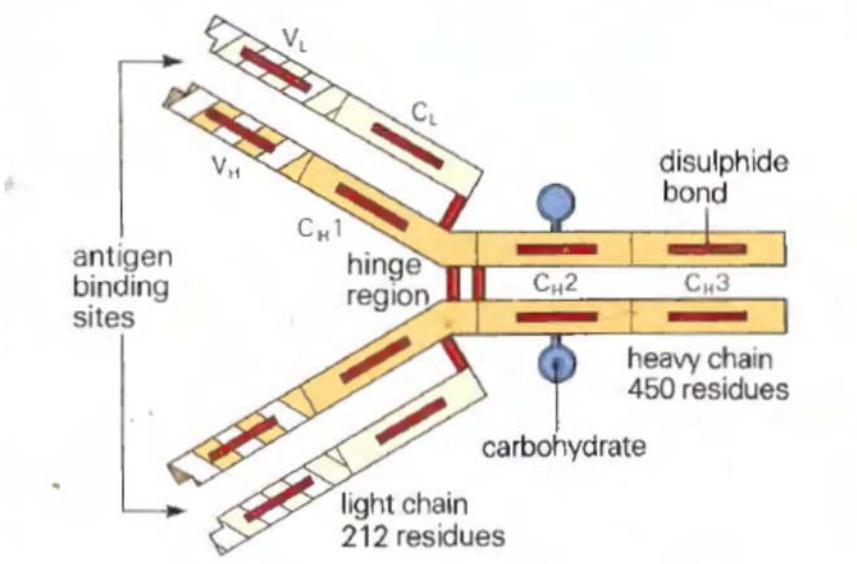
1. The Ordinary Meaning Of The Term "Domain" Excludes The Hinge.

The ordinary meaning of the term "domain," as understood by a POSA in 1990, does not include the hinge region, which is different both structurally and functionally from the domains of an immunoglobulin. "The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). Defendants' expert, Kathryn E. Stein, Ph.D., a former Director of the FDA's Division of Monoclonal Antibodies, who has more forty years of experience in the field of immunology, confirms that "to a POSA, the term 'domain' in the context of immunoglobulins has a plain and ordinary meaning that does not include a hinge." Stein Decl. at ¶¶ 6-9, 25.

As Dr. Stein explains, "[t]he term 'domain' is a scientific term used by immunologists to refer to the structurally distinct globular regions of the three-dimensional structure of an immunoglobulin. A POSA would have known that the constant region of the heavy chain of IgG has one C_H domain in the Fab region (C_{H1},) and two C_H domains in the Fc region (C_{H2} and C_{H3})." Stein Decl. at ¶ 26. A POSA

would have understood that "[t]hese domains do not include the 'hinge,' which is located between the C_{H1} and C_{H2} domains of the heavy chain." *Id.* Thus, to a POSA, the plain an ordinary meaning of "all of the domains of the constant region of a human immunoglobulin IgG [or IgG1] heavy chain other than the first domain of said constant region" would refer to just the CH2 and CH3 domains.

This plain and ordinary meaning of the term "domain" is reflected in the contemporaneous textbooks in the field of immunology. For example, Immunology by Dr. Ivan M. Roitt *et al.*, illustrates the basic structure of IgG in Figure 5.6 (reproduced below).



Id. at ¶ 27 (quoting Stein Ex. 5 at SAN-ETAN_0188433). Dr. Roitt explains that "[t]he constant portion of the heavy chain is further divided into ***three structurally discrete regions: CH1, CH2, and CH3***. These globular regions, which are stabilized by intrachain disulphide bonds, ***are referred to as 'domains.'***" *Id.* (emphasis added).

These three domains do not include the hinge, which "is a segment of the heavy chain between the CH1 and CH2 domains." *Id.*

As another example, the chapter entitled "Immunoglobulins I: Structure & Function," authored by Joel W. Goodman, Ph.D., in the textbook BASIC & CLINICAL IMMUNOLOGY, defines the domains of the heavy chain to include one variable domain and three constant domains:

> **Domains**: The polypeptide chains do not exist 3-dimensionally as linear sequences of amino acids but are folded by disulfide bonds into globular regions called domains. ***The domains in H chains are designated VH, CH1, CH2, and CH3***; and those in L chains are designated VL and CL.

See Stein Decl. at ¶ 28 (quoting Stein Ex. 3 at SAN-ETAN_0188411). The domains of the heavy chain do not include the "hinge region," which is defined as "[t]he area of the [heavy] chains in the [constant] region between the first and second [constant] region domains (CH1 and CH2)." *Id.* Thus, the textbooks in the field of immunology are consistent that the domains do not include the hinge.

In addition, POSAs do not refer to the "hinge" as among the "domains" of the constant region of the heavy chains of IgG because the hinge and domains are structurally and functionally different. As Dr. Stein explains, the theory that the parts of IgG may be characterized as "domains" arose when the study of the IgG structure revealed that certain parts shared structural characteristics, particularly a common size and composition. Stein Decl. at ¶¶ 35-36. By contrast, the "lack of

homology to any constant region domain is a feature of the hinge region." *Id.* at ¶ 36 (quoting Stein Ex. 7 at SAN-ETAN_0188592).

A POSA would have known that the hinge does not share the same size as the domains. By 1989, it was well-known that each of the domains of the human IgG heavy chain has a consistent size of about 100-110 amino acids. *Id.* at ¶ 37. This uniformity in size of the domains of human IgG heavy chain appears to be the "result of duplications of an ancestral immunoglobulin gene, which produced a molecule about 110 residues in length." *Id.* at ¶ 38 (quoting Stein Ex. 7 at SAN-ETAN_0188592). While the domain size is uniform from domain to domain, the hinge size varies depending upon the subclass of IgG. *Id.* at ¶ 39. For instance, although the size of the IgG3 hinge is about 100 amino acids, the size of the IgG1 hinge is about 15 amino acids (significantly smaller than the domains). *Id.*

A POSA would have further known that the hinge does not share the same composition as the domains. Each of the domains of IgG share a distinctive three-dimensional globular or rounded shape, referred to as an "immunoglobulin fold." *Id.* at ¶ 41. The amino acid sequence of each of the IgG domains is folded into anti-parallel β-pleated sheets that are maintained by intrachain disulphide bonds. *Id.* at ¶¶ 41-42. These folds define the bounds of the domain. *Id.* Instead of being folded, in contrast, the hinge is a segment of the immunoglobulin that does not have a

globular shape and does not have an intrachain disulfide bond. *Id.* at ¶ 43. The hinge is a flexible stretch of the amino acid chain, which functions to provide flexibility for the two antigen-binding arms of the immunoglobulin to bind the antigen. *Id.* at ¶ 44. In layman's terms, the hinge's flexibility allows the two arms at the top of the y-shape to conform to the binding target. Thus, the hinge lacks the common structural and functional features, particularly size and configuration, which define the domains of IgG.

Thus, a POSA would have understood that the heavy chain of IgG (or IgG1) has one domain in the variable region (V_H) and three domains in the constant region (C_{H1}, C_{H2}, and C_{H3}). To a POSA, the plain and ordinary meaning of "all of the domains of the constant region of a human immunoglobulin IgG [or IgG1] heavy chain other than the first domain of said constant region [i.e., C_{H1}]" would refer to just the domains C_{H2} and C_{H3} of human IgG [or IgG1]. *Id.* at ¶ 46.

Moreover, the specification does not alter the plain and ordinary meaning of the term. Indeed, the specification does not mention a hinge at all. Plaintiffs cite to Example 11 of the submarine patents as providing an example of a fusion protein that includes a hinge. But Example 11 does not help them.

Example 11 refers to a piece of DNA called pCD4-Hγ3 that may be used to express or generate a fusion protein in which a specific kind of fusion protein is

modified to place two p55 TNFR on the top of the "Y". *See, e.g.*, Bogad Ex. 1, '182 patent, at Example 11. This example does not describe the structure of the fusion protein as including a hinge, however. Rather, it simply references three patent applications: European Patent Application No. 90107393.2; Japanese Application No. 108967/90; and USSN 510773/90.

None of these applications were published at the time of filing and, thus, would not have been available to a POSA at the time of filing. The description of the fusion protein in European Patent Application No. 90107393.2, was not published until October 31, 1990, over a month after the September 10, 1990 priority date. Similarly, the referenced Japanese Application No. 108967/90 did not publish until February 5, 1991 (JP 3035781A). The referenced U.S. application (USSN 510773/90) remains unpublished; it was likely abandoned. Because the meaning of claims is determined at the time of filing, these non-publicly-available references cannot serve to reflect what one skilled in the art would understand at the time of the invention when reading the entire patent. *Helmsderfer v. Bobrick Washroom Equipment, Inc.*, 527 F.3d 1379, 1381 (Fed. Cir. 2008) ("To construe a claim term, a court must determine the meaning of any disputed words from the perspective of one of ordinary skill in the pertinent art at the time of filing."); *Quaker City Gear Works, Inc. v Skil Corp*., 747 F.2d 1446, 1455 (Fed. Cir. 1984) (addressing the issue

of enablement, "[i]ncorporation by reference has never been permissible under 35 U.S.C. § 112 of material necessary for an adequate disclosure which is unavailable to the public.").

In fact, Plaintiffs argued during prosecution that the skilled artisan would have considered a TNFR monomer—*i.e.*, a protein lacking a hinge—not only as a possibility, but as a *preferred structure* for TNFR fusions. Specifically, when arguing against an obviousness rejection, Plaintiffs argued that the skilled artisan would be motivated to construct a monomeric fusion (TNFR-C_{H2}-C_{H3}) lacking a hinge. Bogad Ex. 12, '182 file history, Oct. 3, 2006 Amend. & Req. Reconsid., at 13-14; *see also id.* at 16-17 (arguing that a person of skill in the art would not have expected a dimeric protein to retain TNF-binding activity); Bogad Ex. 10, '182 file history, Feb. 28, 2008 Appeal Brief at 43-44 (arguing same); Bogad Ex. 13, '522 file history, Sept. 8, 2010 Amend & Req. Reconsid. at 26-27 (arguing same); *id.* at 24-25 (discussing various reasons why the person of ordinary skill in the art would prefer constructs without the hinge).

Plaintiffs even argued that deletion of the hinge region would have been desirable because of its potential negative effects and that a person of skill in the art would therefore have been motivated to exclude the hinge:

> Deletion of the hinge region … would also have been desirable from the standpoint of eliminating a part of the constant region involved in

> the pro-inflammatory effector functions. The ordinary skilled artisan would have been motivated to avoid combining such pro-inflammatory activity with an anti-inflammatory TNF-binding agent such as soluble p75 TNFR.

Bogad Ex. 13, '522 file history, Sept. 8, 2010 Amend. and Req. Reconsid., at 26-27. Thus, given the plain and ordinary meaning of the term "domain," a POSA reading the patent specification in 1990, would have understood the claimed fusion protein to be a molecule that excluded the hinge.

2. Plaintiffs' Construction Contradicts The Plain And Ordinary Meaning

Plaintiffs' construction is directly contrary to the plain and ordinary meaning of the term "domain." As discussed, the specification itself contains no description of the hinge but instead uses language similar to the claims to describe the invention: "all domains except the first domain of the constant region of the heavy chain of human immunoglobulin IgG." Bogad Ex. 1, '182 patent, 2:36-39. Based on the plain and ordinary meaning of the term "domain," the specification does not contain a written description of a fusion protein that contains the hinge region.

Plaintiffs attempt to overcome this deficiency by relying on ambiguous extrinsic evidence and the prosecution history. Both efforts fail.

Plaintiffs rely on casual usages of the term "domain" in a few textbooks and articles to argue that the term "domain" includes the hinge. *See* Dkt. No. 119, Joint Claim Construction and Prehearing Statement ("JCCS"), Exhibit A, at 26-28. But,

this completely ignores the significant structural and functional differences between a domain and a hinge described above that make clear that POSAs do not consider hinges to be domains. *See supra*, at Section IV.A.1; Stein Decl. at ¶¶ 34-45.

Plaintiffs also rely heavily on the prosecution history because the specification is silent on the hinge. "To act as its own lexicographer, a patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning. It is not enough for a patentee to simply disclose a single embodiment or use a word in the same manner in all embodiments, the patentee must clearly express an intent to redefine the term." *Thorner*, 669 F.3d at 1365 (quotations and citations omitted); *accord Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1371 (Fed. Cir. 2014) ("The standards for finding lexicography and disavowal are exacting. To act as its own lexicographer, a patentee must clearly set forth a definition of the disputed claim term other than its plain and ordinary meaning' and must 'clearly express an intent to redefine the term.") (quotations and citations omitted). Here, Plaintiffs did not act as their own lexicographers with respect to the word "domain."

Indeed, Plaintiffs contended during prosecution that a person of ordinary skill in the art would have preferred constructs without a hinge. *See supra*, at Section IV.A.1. They should not be allowed to fix a deficient patent specification—one that fails to describe a protein with a hinge—through statements made in prosecution,

after the application was filed. *See Roy-G-Giv Corp. v. ABB, Ltd.*, 63 F. Supp. 3d 690, 696 (E.D. Tex. 2014) ("Thus, as a matter of law, the written description requirement cannot be met by new matter added during prosecution."); *see also Libel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 909 n. 2 (Fed. Cir. 2004) ("[I]t is not improper for an applicant to broaden his claims during prosecution in order to encompass a competitor's products, as long as the disclosure supports the broadened claims.").

B. '182 Patent: The Term "Specifically Binds TNF" Should Be Construed To Require Only In Vitro TNF Binding, Consistent With The Intrinsic Record.

Claim Terms[5]	Immunex's Proposal	Sandoz's Proposal
"specifically binds TNF"	"has the ability to strongly and stably bind human TNF"	"binds a detectable amount of TNF in an *in vitro* TNF binding assay"

Sandoz's construction of "specifically binds TNF" is wholly consistent with the intrinsic record and should be adopted. Indeed, the specification and file history make clear that what is required to meet the claims is *in vitro*, or in the test tube, TNF binding. Plaintiffs' construction is too vague and attempts to import an *in vivo*, or in the body, requirement that is contrary to the intrinsic record.

[5] Bogad Ex. 1, '182 patent at claims 1-36.

The specification makes clear that the claims only require TNF-binding *in vitro*. It explains that the invention is directed to proteins "capable of binding tumor necrosis factor-(TNF)." Bogad Ex. 1, '182 patent, 2:24-25. It further explains that "[t]he TNF binding activity of the proteins of the present invention may be determined using the assay described in Example 1." *Id.* at 3:21-23. The assay in Example 1 is an *in vitro* test or "assay" that a POSA can use to determine whether a protein binds TNF. *Id*. at 10:29-52.

Similarly, the prosecution history repeatedly references and describes *in vitro* testing that the applicants conducted in order to demonstrate purported unexpected results of the claimed invention. Indeed, in response to a rejection for indefiniteness of the term "specifically," the applicants:

> respectfully submit[ted] that one of ordinary skill in the art would have clearly understood the meaning of the term "specifically" after reading the specification. For example, ***Example 1 (page 21, lines 6-22) notes that the desired TNF binding proteins have specific TNF binding activity and discusses an exemplary assay for determining specific TNF binding.***

Bogad Ex. 14, '182 file history, Oct. 5, 2005 Amend & Req. Reconsid. at 9 (emphasis added). Thus, Plaintiffs clearly indicated that the assay of Example 1 could be used to determine specific TNF binding as claimed.

Moreover, in response to an examiner obviousness rejection based on the prior art, the applicants submitted a Declaration by Werner Lesslauer describing *in vitro*

TNF-binding assays conducted with fusion proteins including a p75 TNFR-IgG fusion protein in an attempt to demonstrate unexpected results. Bogad Ex. 15, '182 file history, Jan. 12, 2005 Amend & Req. Reconsid., Decl. of Dr. Werner Lesslauer ("Lesslauer Decl."), Ex. B. The applicants argued that these *in vitro* binding assays demonstrated that the claimed fusion proteins bound TNF and allegedly did so in a surprisingly effective manner. *Id.*; *see also* Bogad Ex. 10, '182 file history, Feb. 28, 2008 Appeal Br. at 54; Bogad Ex. 15, Lesslauer Decl. at Ex. A.

Sandoz's construction is fully supported by the specification and the prosecution history and should be adopted. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("It is well-settled that, in interpreting an asserted claim, the court should look first to the intrinsic evidence of record, *i.e.*, the patent itself, including the claims, the specification and, if in evidence, the prosecution history. Such intrinsic evidence is the most significant source of the legally operative meaning of disputed claim language.") (internal citations omitted).

Plaintiffs' construction, in contrast, is too vague to be useful. It provides no guidance as to what "strongly and stably bind" means and fails to make clear that *in vitro* binding is what is required to meet the claims. *See, e.g.*, *Dayco Prods., Inc. v. Total Containment, Inc.*, 258 F.3d 1317, 1324 (Fed Cir. 2001) ("In an effort to support the district court's claim construction and decision, the appellee invites us

to embark on a speculative and convoluted reading of the claim language, the specification, and the prosecution history.").

As an initial matter, the specification contains no evidence that the claimed fusion proteins would bind TNF *in vivo*. It contains no description that the claimed fusion protein was made or was tested in any human or animal subject to determine whether it binds TNF. No *in vivo* testing protocol is provided, nor are results from *in vivo* tests. To the contrary, the specification expressly states that uses other than *in vivo* uses are contemplated for the claimed invention. For instance, the '182 patent describes the use of the claimed inventions for diagnostic purposes, which would not typically be *in vivo*:

> On the basis of the high binding affinity of the TNF-BP in accordance with the invention for TNF . . . these or fragments thereof can be used as diagnostics for the detection of TNF in serum or other body fluids according to methods known in the state of the art[.]

Bogad Ex. 1, '182 patent, 9:66-10:3.

In addition, Plaintiffs presented no evidence during prosecution regarding the TNF-binding abilities of TNFR fusion proteins *in vivo*. Yet, Plaintiffs apparently arrive at their construction of "strongly and stably bind" based on what *would* happen *in vivo*: "The human body has many cytokines which mediate their biological activities by strongly and stably binding to their particular receptors." JCCS, Ex. A at 66. Not only does the specification not mention strong and stable

binding *in vivo*, but also Plaintiffs provide no explanation for what "strongly and stably bind" means or how to measure the extent to which TNF-binding must occur in order to "strongly and stably bind" TNF.

Plaintiffs are improperly inviting the Court to construe the claims in a way that raises more claim construction disputes later. *Paragon Solns., LLC v. Timex Corp.*, 566 F.3d 1075, 1089 (Fed. Cir. 2009) (rejecting a proposed construction that "is no more or less clear than" the disputed claim term, and "is therefore unhelpful in ascertaining the meaning" of the disputed claim term). Plaintiffs' construction should be rejected and Sandoz's adopted.

C. '522 Patent: The Polynucleotide Term Requires That The Polynucleotide Encode Only The Claimed Protein

Claim Terms[6]	Immunex's Proposal	Sandoz's Proposal
"wherein the polynucleotide encodes a protein consisting of"	"wherein the polynucleotide contains the genetic information for a protein consisting of"	"the polynucleotide encodes only the protein and includes no other amino acid sequence"

The '522 patent claims each contain the phrase "wherein the polynucleotide encodes a protein consisting of." Under controlling Federal Circuit case law, "[t]he phrase 'consisting of' is a term of art in patent law signifying restriction and

[6] Bogad Ex. 2, '522 patent claims 1-3, 7-10.

exclusion…. In simple terms, a drafter uses the phrase 'consisting of' to mean 'I claim what follows and nothing else.'" *Vehicular Techs. Corp. v. Titan Wheel Intern., Inc.*, 212 F.3d 1377, 1382-83 (Fed. Cir. 2000) (internal citations omitted). Accordingly, the plain and ordinary meaning of the term "wherein the polynucleotide encodes a protein consisting of" is to encode the protein and nothing else.

Plaintiffs' construction fails to address the "consisting of" language and instead simply rewords the term "encodes" as "contains the genetic information for." In other words, Plaintiffs' construction adds nothing to illuminate the meaning of the term. As Sandoz's construction is consistent with controlling Federal Circuit case law, it should be adopted.

D. Psoriasis Patents: "Patient"

Claim Term[7]	Immunex's Proposal	Sandoz's Proposal
"patient"	"human in need of treatment"	"any animal, including a non-human animal"

The term "patient" in the claims is expressly defined in the specification to include any animal. Accordingly, Sandoz's construction is correct and Plaintiffs', which limits the term to humans, is not. *See Sinorgchem Co., Shandong v. Int'l*

[7] Bogad Ex. 3, '225 patent claims 1-9, 12-16, 20; Bogad Ex. 4, '605 patent claims 1-4, 10-13; Bogad Ex. 5, '631 patent claims 1-15, 17-22.

Trade Comm'n, 511 F.3d 1132, 1138 (Fed. Cir. 2007) ("a definition set forth in the specification governs the meaning of the claims,"); *Multiform Desiccants, Inc. v. Medzam, Ltd.,* 133 F.3d 1473, 1478 (Fed. Cir. 1998) ("When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term.").

The psoriasis patents' specification states: "[t]he invention provides compounds, compositions, and methods for treating ***a mammalian patient, including a human patient,*** who is suffering from a medical disorder characterized by abnormal or elevated expression of TNF-α." Bogad Ex. 3, '225 patent at 3:58-61[8] (emphasis added). The specification further states: "***[i]n addition to human patients***, inhibitors of TNF-α are useful in the treatment of autoimmune and inflammatory conditions ***in non-human animals, such as pets (dogs, cats, birds, primates, etc.)***, ***or any animal*** that suffers from a TNF-α mediated inflammatory or arthritic condition." *Id.* at 15:61-66 (emphasis added). Both psoriasis and psoriatic arthritis are such "autoimmune and inflammatory conditions."

The specification also provides a method for calculating the appropriate dose of TNF inhibitor for a wide variety of non-human animals: "the dose is determined

[8] As the Psoriasis Patents share a specification, only citations to the '225 patent will be provided, unless otherwise necessary and specifically noted.

according to the animal's surface area…[f]or small animals, such as dogs or cats a suitable dose is 0.4 mg/kg." *Id.* at 15:66-16:12. This specification then discloses that TNFR:Fc may be used to treat non-human animals: "In a preferred embodiment, TNFR:Fc [Enbrel®][9] (preferably constructed from genes derived from the same species as the patient), or another soluble TNFR mimic, is administered by injection or other suitable route one or more times per week until the animal's condition is improved, or it may be administered indefinitely." *Id.* at 16:6-11.

Nowhere does the specification limit "patient" to humans. Had Plaintiffs intended to do so, they could have used the term "human" or "human patient" in the claims. They did not. Instead, they sought a broad claim covering a "patient" with no modifier with a specification that disclosed that the patient could include any range of animals, including humans.

Thus, there is absolutely no basis, either in the specification or in the claims, to limit the claim term "patient" to only humans. "Varied use of a disputed term in the written description demonstrates the breadth of the term rather than providing a

[9] "TNFR:FC" is expressly defined in the specification, which states as follows: "A preferred TNFR-Ig fusion protein suitable for treating diseases in humans ***and other mammals*** is recombinant TNFR:Fc, a term which as used herein refers to 'etanercept,' which is a dimer of two molecules of the extracellular portion of the p75 TNF□ receptor, each molecule consisting of a 235 amino acid TNFR-derived polypeptide that is fused to a 232 amino acid FC portion of human IgG1. Etanercept is currently sold by Immunex Corporation under the trade name ENBREL®. Bogad Ex. 3, '225 patent at 4:44-52 (emphasis added).

limited definition." *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 991 (Fed. Cir. 1999). Sandoz's proposed construction is proper because, unlike Plaintiffs', it is consistent with the breadth of the term "patient" as used in the specification.

E. Psoriasis Patents: "Psoriasis" & "Ordinary Psoriasis"

Claim Term[10]	Immunex's Proposal	Sandoz's Proposal
"psoriasis"	"a particular human inflammatory disease of the skin and/or nails, as diagnosed by physicians"	"an inflammatory disease of the skin and/or nails that does not include the symptoms of psoriatic arthritis," or indefinite under 35 U.S.C. § 112
"ordinary psoriasis"	"psoriasis without the more serious symptoms of psoriatic arthritis"	"an inflammatory disease of the skin and/or nails that does not include the symptoms of psoriatic arthritis," or indefinite under 35 U.S.C. § 112

Sandoz's proposed construction for "psoriasis" and "ordinary psoriasis" is proper because it is consistent with the claims and specification, statements the applicant made during prosecution, and is the only way to construe such claim terms such that they "provide objective boundaries for those of skill in the art when read in light of the specification and the prosecution history." *Liberty Ammunition, Inc.*

[10] Bogad Ex. 3, '225 claims 1-9, 12-16, 20 ("psoriasis"); Bogad Ex. 4, '605 claims 1-4, 10-13 ("ordinary psoriasis").

v. United States, 835 F.3d 1388, 1396 (Fed. Cir. 2016) (internal quotations and citations omitted.)

1. Sandoz's Construction Recognizes that Psoriasis and Psoriatic Arthritis Are Separate Diseases

The specification of the psoriasis patents makes clear that psoriasis or "PsO" is a separate and distinct disease from psoriatic arthritis, or "PsA." According to the specification, "[p]soriasis and PsA are different clinical entities, and are associated with somewhat different MHC haplotypes." Bogad Ex. 3, '225 Patent at 1:58-60.

Psoriasis is an inflammatory disease of the skin and nails, as explained in the specification, that is "characterized by epidermal keratinocyte [skin cell] hyperproliferation [overgrowth], accompanied by neutrophil and T cell infiltration, and is associated with elevated levels of inflammatory cytokines, including TNF-α, IL-6 and TGF-β…." *Id.* at 1:53-57; *see also id.* at 12:34-48; 16:55-17:8 ("…at least one psoriatic lesion of the ***skin or nails***.") (emphasis added); *Id*. at 14:14-28 (defining "ordinary psoriasis" as including "pitted fingernails, with or without yellowish discoloration, crumbling nails, or inflammation and detachment of the nail from the nail bed (nail psoriasis)."). Psoriatic arthritis, on the other hand, is an inflammatory disease of the joints. According to the specification, "[f]or purposes of this invention, patients are defined as having psoriatic arthritis (PsA) if they have

one or more swollen joints or one or more painful or tender joints, and also manifest at least one psoriatic lesion of the skin or nails." *Id.* at 12:34-39.

The claims of the patents also make clear that the two diseases are distinct. For example, dependent claim 12 of the '225 patent recites "[a] method for treating a patient having psoriasis and psoriatic arthritis…." *Id.* at claim 12. Also, claim 1 of the '631 patent covers treating a patient "having psoriatic arthritis *and/or* plaque psoriasis." Bogad Ex. 5, '631 patent at claim 1 (emphasis added).

The patentee further clarified that these diseases were distinct entities during the prosecution of the '605 patent. Plaintiffs' claims to a method of treating "psoriasis" were rejected over prior art that disclosed treating psoriatic arthritis. Bogad Ex. 16, '605 file history, May 3, 2011 Non-final rejection, at 2-5. The applicant summarized the Examiner's rejection as follows: "'The Action further states that treating a patient with PsA overlaps treating a patient with PsO or, 'to put it another way, treating a patient with psoriasis is generic to treating a patient with psoriasis and psoriatic arthritis. Therefore, treating a patient having psoriasis or having psoriasis and psoriatic arthritis with TNFR:Fc is prima facie obvious.'" *Id.*; Bogad Ex. 17, '605 file history, Aug. 5, 2011 Amend and Req. Reconsid., at 4.

In response to this rejection, the applicant amended the claims to recite "ordinary psoriasis" instead of "psoriasis" and argued:

> PsA is a form of chronic arthritis that is usually associated with PsO at some time during the course of the disease. As discussed and supported below, PsA is not always and necessarily accompanied by PsO at any particular moment in the disease process. In fact, there is a condition called psoriatic arthritis sine psoriasis, i.e., PsA without PsO. Therefore, treatment of PsA does not necessarily imply that PsO is simultaneously being treated and vice versa.

Id. at 4-5.

Thus, Plaintiffs again made clear during prosecution that psoriasis and psoriatic arthritis are distinct diseases, and that a patient may have one without having the other at any given time. Therefore, any construction, such as Plaintiffs' proposed construction, that blurs the lines between psoriasis and its symptoms, and psoriatic arthritis and its symptoms, is inconsistent with the patent claims and file history. Further, nothing in the specification limits "psoriasis" to being a human disease, nor does the specification state that one must be *diagnosed* with psoriasis in order to actually have psoriasis.

Regarding the term "ordinary psoriasis," the file history, discussed above, makes clear that "ordinary psoriasis" is a term that is used for a patient that has "psoriasis," but that has not been previously or concomitantly diagnosed with "psoriatic arthritis." Plaintiffs agree that "a patient with 'ordinary psoriasis' will lack certain symptoms exhibited by a patient with 'psoriatic arthritis.' Nonetheless, like patients with 'psoriatic arthritis,' patients with 'ordinary psoriasis' have 'psoriasis.'" Plaintiffs' L. Pat. R. 3.4A Disclosure at 357.

2. Sandoz's Constructions Avoid Confusion and Overlap Between Terms, Which Would Render These Terms Indefinite

Blurring the lines between the definitions of these claim terms, as Plaintiffs' proposed constructions do, makes each of these terms indefinite. The specification is rife with inconsistent statements about these diseases that appear to be directly inconsistent with the language of the claims. For example, the specification states that "treatments used for the psoriatic lesions of PsA generally are similar to those used to treat psoriasis." Bogad Ex. 3, '225 patent at 1:65. This statement blurs the distinction between psoriasis and psoriatic arthritis. But the very next sentence in the specification reads: "[p]soriatic skin lesions are present in patients with PsA, although only a minority of psoriasis sufferers actually have PsA." *Id.* at 1:65-67. This sentence distinguishes between psoriasis and PsA as separate diseases that can occur, in some instances, at the same time in the same patient. Again, appearing to blur the two diseases, the specification states that patients with "active psoriatic arthritis (PsA)" were enrolled in a study to determine whether administration of TNFR:Fc would be effective "for both the arthritic and psoriatic aspects of this disease [PsA]" (*id.* at 16:18-24), and the specification also refers to "the psoriatic aspects of PsA" (*id.* at 17:62-63).

Blurring or overlap of the definitions for psoriasis and psoriatic arthritis, in view of the confusing statements in the specification, would leave a person of

ordinary skill in the art with no "objective boundaries for those of skill in the art when read in light of the specification and the prosecution history." *Liberty Ammunition, Inc.*, 835 F.3d at 1396 (quotations and citation omitted).

Only Sandoz' proposed constructions for the claim terms "psoriasis" and "ordinary psoriasis" (and for "psoriatic arthritis," below) as distinct and separate entities avoids confusion and allows a reasonable determination of claim scope. Thus, Sandoz's construction for the terms "psoriasis" and "ordinary psoriasis" should be adopted.

F. Psoriasis Patents: "Psoriatic Arthritis"

Term[11]	Immunex's Proposal	Sandoz's Proposal
"psoriatic arthritis"	"a particular human inflammatory disease, as diagnosed by physicians, characterized by one or more swollen joints or one or more painful or tender joints, and also manifest at least one psoriatic lesion of the skin or nails before or after the onset of joint symptoms"	"an inflammatory disease characterized by one or more swollen joints or one or more painful or tender joints, and also manifest at least one psoriatic lesion of the skin or nails prior to or concurrent with the onset of joint symptoms," or indefinite under 35 U.S.C. § 112

The psoriasis patents expressly define psoriatic arthritis: "[f]or purposes of this invention, patients are defined as having psoriatic arthritis (PsA) if they have

[11] Bogad Ex. 3, '225 patent claims 12-15; Bogad Ex. 5, '631 patent claims 1-5, 7, 17-22.

one or more swollen joints or one or more painful or tender joints, and also manifest at least one psoriatic lesion of the skin or nails. The psoriatic lesions may appear before or after the onset of swollen or tender joints…." Bogad Ex. 3, '225 patent, at 12:34-48 (emphasis added). This should end the matter. The specification expressly defines the claim term and there is no intrinsic evidence to cast this definition in doubt, except for inconsistent specification statements that, as discussed above with respect to the claim terms "psoriasis" and "ordinary psoriasis," would render the term "psoriatic arthritis" indefinite if interpreted otherwise. *See Sinorgchem,* 511 F.3d at 1138.

In addition, as with Plaintiffs' construction of "psoriasis" and "ordinary psoriasis" Plaintiffs' addition of "as diagnosed by a doctor" is unwarranted and unsupported by either the claim language or the intrinsic record.

G. Psoriasis Patents: "Plaque Psoriasis"

Term[12]	Immunex's Proposal	Sandoz's Proposal
"plaque psoriasis"	"a subtype of psoriasis, characterized by inflamed swollen skin lesions covered with silvery white scale"	"an inflammatory disease of the skin characterized by inflamed swollen skin lesions covered with silvery white scale"

As with "psoriatic arthritis" the psoriasis patents expressly define plaque psoriasis as presenting with "inflamed swollen skin lesions covered with silvery

[12] Bogad Ex. 5, '631 patent claims 1-6, 8-15.

white scale." Bogad Ex. 3, '225 patent at 14:14-28. Again, this ends the matter. *See Sinorgchem,* 511 F.3d at 1138. Nothing in the specification limits plaque psoriasis to humans, and nothing in the specification states that you must be diagnosed with plaque psoriasis to actually have plaque psoriasis. Sandoz's construction is proper because it tracks the definition for "plaque psoriasis" provided in the specification without improperly attempting to import additional, unsupported limitations into the definition.

V. CONCLUSION

For the foregoing reasons, Sandoz requests that the Court adopt its proposed constructions of the disputed claim terms, which apply their plain and ordinary meaning to a POSA, consistent with the intrinsic record.

Dated: December 1, 2016

WINSTON & STRAWN LLP
Attorneys for Defendants Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH

By: */s/ Melissa Steedle Bogad*
James S. Richter
jrichter@winston.com
Melissa Steedle Bogad
mbogad@winston.com

Of Counsel:
George C. Lombardi
Maureen L. Rurka
Julia Mano Johnson
WINSTON & STRAWN LLP
35 W. Wacker Drive
Chicago, IL 60601
(312) 558-5600

Merritt D. Westcott
Melinda K. Lackey
WINSTON & STRAWN LLP
1111 Louisiana, 25th Floor
Houston, TX 77002

CERTIFICATION OF SERVICE

The undersigned attorney certifies that copies of the foregoing **DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF** and supporting documents were served by ECF on December 1, 2016, upon all counsel of record.

/s/ Melissa Steedle Bogad

Melissa Steedle Bogad
mbogad@winston.com

Dated: December 1, 2016